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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/522,986	09/13/2006	Piero Del Soldato	026220-00061	6969
4372	7590	06/25/2008		
ARENT FOX LLP 1050 CONNECTICUT AVENUE, N.W. SUITE 400 WASHINGTON, DC 20036			EXAMINER LAO, MARIALOUIA	
			ART UNIT 1621	PAPER NUMBER
			NOTIFICATION DATE 06/25/2008	DELIVERY MODE ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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IPMatters@arentfox.com
Patent_Mail@arentfox.com

Office Action Summary	Application No. 10/522,986	Applicant(s) DEL SOLDATO ET AL.	
	Examiner Louisa Lao	Art Unit 1621	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 02 May 2008.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-4 and 6-26 is/are pending in the application.
- 4a) Of the above claim(s) 2 and 11-23 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1,3-4,6-10 and 24-26 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Response to Arguments

1. Applicant's arguments filed 5/2/08 are addressed, as follows, with respect to the:
 - a. cancellation of claim 5, not claim 6, is acknowledged; claims 1-4 and 6-26 are pending, and not claims are 1-23 only; where claims 2 and 4-23 had been withdrawn from consideration as of the last Office Action 5/2/08.
 - b. objections of claims (3 and 4) and (4 and 6-10) in light of the amendments were persuasive. The objections had been withdrawn in the last Office Action 5/2/08. Hence, there are no outstanding objections, as stated by Applicants.
 - c. rejection of claims 1, 3-4, 6-10 and 24-26 under 35 U.S.C. 103(a), have been considered, but they are not persuasive, see below. The rejection is maintained.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

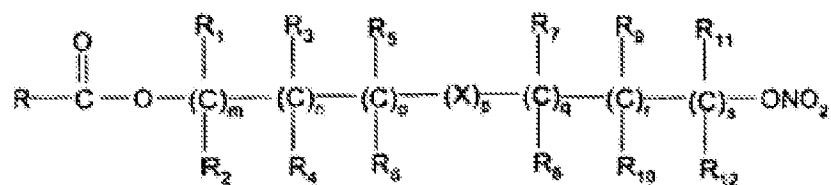
This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor

Art Unit: 1621

and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

2. The rejection of claims 1, 3-4, 6-10 and 24-26 is maintained under 35 U.S.C. 103(a) as being unpatentable over Del Soldato (US5861426, US`426 equivalent to WO95/30641 *in ISR*) or Del Soldato et al. (US7199258, US`258).

3. Applicants' claims are drawn to a process for preparing a compound of the general

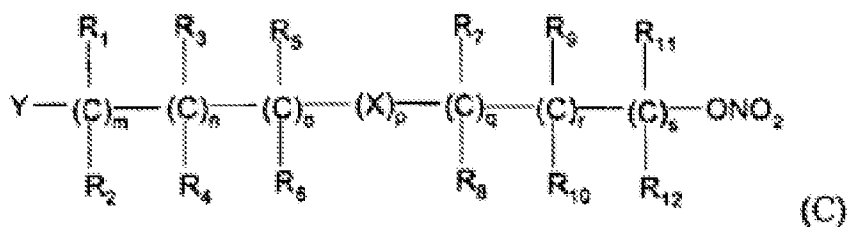


(A)

formula , with the

substituents defined therein. The process comprising the reaction of a compound of formula (B)

R-COO-Z, with a compound of formula (C), as shown



(C)

, and the substituents as

recited therein.

Art Unit: 1621

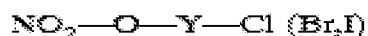
4. US'426 teaches nitro compounds of the formula $A-X_1-NO_2$ (see Abstract).

New compounds and their compositions having anti-inflammatory, analgesic and anti-thrombotic activities, of the general formula: $A-X_1-NO_2$ or their salts, wherein: A is $R(COX_u)_t$, wherein t is zero or 1 and u is zero or 1; and X is O, NH or NR_{1C} wherein R_{1C} is C_1-C_{10} alkyl; and R is (Ia) wherein R_1 is acetoxoy, preferably n ortho-position with respect to $-CO-$ and R_2 is hydrogen; or derivatives of acetylsalylsalicylic acid; and X_1 is $-YO-$ wherein Y is C_1-C_{20} alkylene, C_5-C_7 cycloalkylene, oxy-alkyl derivatives and oxy-methyl benzyl derivatives.

In columns 15- 16, US'426 teaches the synthetic route by which these compounds are achieved.

In particular, US'426 teaches in column 16 lines 3-14

An alternative route to form the esters is a reaction of the sodium or potassium salts of the acids with the nitric esters of halogen alcohols of the general formula:



to directly give the products of the invention.

The reaction route is as follows:



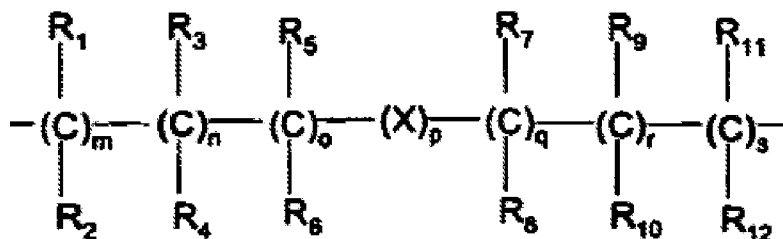
wherein YO is X_1 .

The synthetic scheme outlined by US'426 *generically embraces the instant process*, as well as teaching structurally similar compounds. The structurally similar compounds are correspondingly where $R-CO-O-Na$ is instant compound of formula [B] and $Br-Y-NO_2$ is instant compound of formula [C] and $R-CO-O-Y-NO_2$ is compound of formula [A].

5. Applicants' process differs from the prior art in that the prior art is directed to a broader genus. US'246 differs from the instant claims in the substituents of the instant compounds of

Art Unit: 1621

formula [B], formula [C] and formula [D] ; illustratively, X₁ of US`246 corresponds to formula



[C]

6. This difference would not have been patentable because it would have been obvious, at the time of that Applicants' invention was made, to one of ordinary skill in the art to have employed a method to prepare nitrooxyester compounds or derivatives thereof with the teachings of US`246; with a reasonable expectation that the sub-genus would have a utility of the genus as a whole.

7. Further, US`258 is relied upon to teach a process for preparing nitrooxyderivatives of naproxen, of general formula (A), comprising reacting a compound of formula (B) with compound of formula (C) (col2-5). US`258 teaches the reaction in examples (Examples 1-4). See also claims 1-8, where US`258 teaches the reaction conditions, solvents and molar ratios,

8. The artisan would have been motivated to use alternate or equivalent materials to arrive at other nitrooxyderivatives of general formula (A), to start with the teachings of US`246 coupled with US`258 since US`258 has shown that the reaction of compounds of formula (B) with formula (C) lead successfully to compounds of formula (A); and the artisan would reach a reasonable expectation that in utilizing equivalent alkoxyaryl-compounds for R that he can make other nitrooxyderivatives of general formula (A) or naproxen.

9. No claims are allowed.

Art Unit: 1621

- Applicants' arguments are the reiteration of those presented in the communication dated 2/12/08. Applicants re-allege that the teachings of the cited prior art reference was because of hindsight and that one of ordinary skill in the art would have no motivation to utilize the teachings of US'246 to arrive at the instant process; since Y in the instant process does not include Cl, Br and I.

However, as pointed out in the Office Action mailed 5/2/08, Applicants' allegations are flawed because US'246 embraces the instant process and shows the mechanics thereto. It would not be inconceivable by one of ordinary skill in the art to start with the teachings of US'246; since US'246 in view of US'258 teaches the process of making nitro-oxyl derivatives; and shows alternate schematic routes thereto.

- The claims would have been obvious because "a person of ordinary skill has good reason to pursue the known options within his grasp, *such as the adaptation of techniques that have been proven to work in his field of endeavor, including the use of equivalent materials as prompted by material availability and costs.* If this leads to the anticipated success, it is likely the product not of innovation but of ordinary skill and common sense."
- The Supreme Court in *KSR* noted that if the actual application of the technique would have been beyond the skill of one of ordinary skill in the art, then the resulting invention would not have been obvious because one of ordinary skill could not have expected to achieve it.

Also, claims 4 and 6 still recite the limitations of Y, that Applicant contends to have been amended and thus not reflective of the prior art's reactants.

Applicants' arguments are unpersuasive.

Conclusion

10. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. Kawashima et al. J.Med.Chem. 1993, 36, 815-819, Ogawa et al. PharmBull Japan 1993 June 1049-54.

11. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37

Art Unit: 1621

CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Louisa Lao whose telephone number is (571)272-9930. The examiner can normally be reached on Mondays to Thursdays from 8:00am to 8:00pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler can be reached on 571-272-0871. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

0614-06192008mll

Louisa Lao

Examiner

Art Unit 1621

/Karl J. Puttlitz/

Primary Examiner, Art Unit 1621